PD2I ELECTROPHYSIOLOGICAL ANALYZER

RELATED APPLICATIONS

This is a divisional of application Ser. No. 08/641,944, filed May 2, 1996.

FIELD OF INVENTION

The invention relates to methods and apparatus for evaluating electrophysiological potentials such as from the electrocardiogram and the electroencephalogram. More specifically, the invention is a method and associated apparatus for evaluating electrophysiological potentials in a manner that will sensitively and specifically predict future pathological events such as cardiac arrhythmias and epilepsy, and monitor altered states of cognition, such as those underlying memory.

BACKGROUND

The recording of electrophysiological potentials has been available to the field of medicine since the invention of the string galvenometer. Since the 1930's electrophysiology has been useful in diagnosing cardiac injury and cerebral epilepsy. The state-of-the-art in modern medicine shows that analysis of R—R intervals observed in the electrocardiogram or of spikes Seen in the electroencephalogram can predict future clinical outcomes, such as sudden cardiac death or epileptic seizures.

Such analyses and predictions are statistically significant when used to discriminate outcomes between large groups of patients who either do or do not manifest the predicted outcome, but known analytic methods are not very accurate when used for individual patients. This general failure of known analytic measures is attributed to the large numbers of false predictions; i.e. the measures have low sensitivity and specificity in their predictions. It is usually known that something "pathological" is going on in the biological system under study, but currently available analytic methods are not sensitive and specific enough to permit utility in the individual patient.

The inaccuracy problems prevalent in the art are due to current analytic measures (1) being stochastic (i.e. based on random variation in the data), (2) requiring stationarity (i.e. the system generating the data cannot change during the recording), and (3) being linear (i.e. insensitive to nonlinearities in the data which are referred to in the art as "chaos").

A need exists in the art for an analytic measure that (1) is deterministic (i.e. based on caused variation in the data), (2) does not require stationarity (i.e. actually tracks nonstationary changes in the data), and (3) is sensitive to chaotic as well as nonchaotic, linear data.

Many theoretical descriptions of dimensions are known such as "D0" (Hausdorff dimension), "D1" (information dimension), and "D2" (correlation dimension). Packard et al., *Geometry from a time series*, Physical Review Letters, 45:712–716 (1980), first suggested that the dimension of the generator could be reconstructed from a time-series sample of data from only one of the variables. Takens, *Detecting strange attractors in turbulance*, Lecture Notes in Mathematics, 898:366–381 (1981) provided a mathematical proof of Packard's idea, Packard et al., Id.; and Grassberger et al., *Characterization of strange attractors*, Physical Review Letters, 50(5):346–349 (1983), developed a simple algorithm called "D2" for calculating the reconstructed dimension.

D2 enables the estimation of the dimension of a system or its number of degrees of freedom from an evaluation of a sample of data generated. Several investigators have used D2 on biological data (Babloyantz, *Complex Systems*, H. Haken (Ed.), Springer Pub., Berlin, pp. 116–122 (1985); Albano et al., *Dimensions and Entropies in Chaotic Systems*, G. Mayer-Kress (Ed.), Springer Pub., Berlin, pp. 231–240 (1986). However, Mayer-Kress et al., *Dimensional analysis of non-linear oscillations in brain, heart and muscle*, Mathematical Biosciences, 90:155–182 (1988), showed that the presumption of data stationarity cannot be met.

Farmer et al., *Dimension of chaotic attractors*, Physica D., 7D:153–180 (1983), proposed the Pointwise Scaling Dimension or "D2i" which Mayer-Kress et al., Id., states was less sensitive to the nonstationarties inherent in data from the brain, heart or skeletal muscle. Mayer-Kress et al., Id., state that D2i is perhaps a more useful estimate of dimension for biological data than the D2, but still has considerable errors of estimation that might be related to data nonstationarities.

Skinner et al., *The correlation-dimension of the heartbeat is reduced by myocardial ischemia in conscious pigs*, Circulation Research, 68:966–976 (1991), describes the Point Correlation Dimension algorithm (PD2) and shows that it is superior to both the D2 and D2i in detecting changes in dimension in nonstationary data (i.e. data made by linking subepochs from different chaotic generators).

Rapp, *A Guide to Dynamical Analysis*, Integrarive Physioiogical and Behavioral Science, 29:3 (1994), lists the ways one can get false impressions about detecting chaos in biological systems. Uncontrolled shifts in the generator which are nonstationarity invalidate measures of the correlation dimension. Furthermore filtered noise can be low-dimensional, have high determinism and contain at least one positive Lyapunov exponent. Oversampling of data can produce spurious low-dimensional estimates due to the presence of too many near neighbors. Undersampling can produce stroboscopic effects that also produce spurious results. Nonstationarity, filter-effects, the presence of noise, a high or low digitization rate, short data epochs are all problems in data acquisition that can lead to spurious results.

Theiler, *Spurious dimension from correlation algorithms applied to limited time-series data*, Physical Reviews, A 34:2427–2432 (1986), describes an algorithm that eliminates near-neighbor effects. Theiler et al., *Testing for nonlinearity in time series: the method of surrogate data*, Physica D., 58: 77–94 (1992), teaches a way to convert the biological data into filtered noise of the same bandpass so that the analysis of the biological data can be compared to this surrogate to rule out the possibility that the data are filtered noise. Others who have used data surrogates as controls include, Schiff et al., *Discriminatina Deterministic versus Stochastic Dynamics in Neuronal Activity*, Integrative Physiological and Behavioral Science, 29:3 (1994).

Skinner et al., *The Point Correlation Dimension: Performance with Non-Stationary Surrogate Data and Noise*, Integrative Physiological and Behavioral Science, 29:3 (1994), discloses an algorithm for calculating the correlation dimension at a small point in the data series. This algorithm resolves two issues at once, (1) it is insensitive to data nonstationarities, and (2) it enables dimension to be calculated as a function of time, thus revealing where the nonstationary shifts are.

New tabulations suggests that although many earlier biological studies may not have been properly conducted or adequately controlled, the original interpretations may have